

Amendments to the Specification:

Please replace the title of this application beginning at page 1, line 1, with the following rewritten title:

-- ~~DERMAL~~ CYTOCHROME P450 INHIBITORS AND ENHANCERS --

Please replace the paragraph beginning at page 3, line 1, with the following rewritten paragraph:

-- The CYP1A subfamily contains two members, CYP1A₁ and CYP1A₂. CYP1A₁ and CYP1A₂ are best known for their activities to catalyze the activation of procarcinogens such as polycyclic aromatic hydrocarbons and aromatic N-arylamines, respectively, enhancing chemically induced carcinogenesis in animals and in humans. (Ioannides et al., Drug Metab. Rev. (1993), 25:453-484). CYP1A₂ is constitutively present in human liver. (Sesardic et al., Carcinogenesis (1990), 11:1183-1188). However, whether CYP1A₁ is also constitutively expressed in human liver is disputed, even though CYP1A₁ is known to be expressed in skin. (Li et al., Carcinogenesis (1995), 16:519-524). Several studies have demonstrated that expression of CYP1A₁ can be induced by xenobiotics in rat skin as well as cultured keratinocytes. (Mukhtar et al., Drug metab. Dispos. (1981), 9:311-314; Bickers et al., J. Pharmacol. Exp. Ther., (1992), 223:163-168). Regulation of CYP1A₁ expression is thought to play a critical role in carcinogenesis, since many chemicals which induce skin CYP1A₁ expression are also initiators of skin tumors in man. (Kinoshita et al., Cancer Res.(1972), 32:1329-1339).--

Please replace the paragraph beginning at page 19, line 5, with the following rewritten paragraph:

-- Determination of Enzymatic Activity of 7-ethoxyresorufin-O-deethylase (CYP1A₁) and 7-methoxyresorufin-O-demethylase (CYP1A₂) and Determination of Inhibition or Enhancement of CYP1A Enzymatic Activity

The enzymatic activity of CYP1A was determined based on the activity of 7-ethoxyresorufin-O-deethylase (i.e., for CYP1A₁) and 7-methoxyresorufin-O-demethylase (i.e., CYP1A₂). The microsomal suspension having protein of about 0.125 mg was reacted in 0.1M

Hepes Buffer (pH = 7.8), 5.7 mM Glucose-6-phosphate, 1.4 unit of Glucose-6-phosphate dehydrogenase, 5.7 mM Magnesium chloride, 1.8 mg/ml bovine serum albumin, 1.9 μ M 7-ethoxyresorufin or 7-methoxyresorufin, and 12.9 μ l CYP1A1 or CYP1A2 activity inhibitor or enhancer, and the total volume of the reaction mixture was 1.2879 ml. Except for the blank group, the reaction was triggered by adding 0.54 μ M NADPH. In the test tube (16 x 100 mm), the reaction was carried out for ten (10) minutes at constant temperature (37°C) with vibration and without light. Methanol 2.5 ml was added into the reaction mixture to stop the reaction. Protein precipitate was removed from the reaction mixture by centrifuging the reaction mixture at 180 xg for ten (10) minutes. The supernatant was tested for florescent intensity with 550 nm as the excitation wavelength and 585 nm the emission wavelength. The florescent intensity was compared with 0.01 μ M - 0.1 μ M standard Rhodamine B solution to obtain the reading of the CYP1A enzyme activity.--